

# Longitudinal DTI changes following cognitive training therapy in a mild traumatic brain injury rat model

K. Braeckman<sup>1</sup>, B. Descamps<sup>1</sup>, K. Caeyenberghs<sup>2</sup>, C. Vanhove<sup>1</sup>

<sup>1</sup>Medical Imaging and Signal Processing group, UGent, Ghent, Belgium, <sup>2</sup>The Mary MacKillop Institute for Health Research, Australian Catholic University, Melbourne, Australia

## Introduction

Traumatic brain injury (TBI) is the leading cause of acquired disability [1]. Cognitive training therapy is part of a multi-modality rehabilitation program to ameliorate difficulties that TBI patients experience [2]. However, the effect of a cognitive training program on tissue microstructure is far from understood in TBI [3]. Therefore, we will characterise microstructural changes induced by cognitive training therapy using diffusion tensor imaging (DTI) in a mild TBI (mTBI) rat model and evaluate whether the type of training (memory vs attention) has an influence on recovery following mTBI.

## Materials and methods

Thirty female Wistar rats ( $256\text{g} \pm 9\text{g}$ ) sustained mTBI and ten did not (healthy control, only scanned, HC). One day after injury the thirty injured rats were randomized into three groups: 20 rats received cognitive training making use of a touchscreen system (i.e. Paired Associate Learning (PAL, memory) or 5-Choice Continuous Performance (CCP, attention training)) and 10 were allowed to recover spontaneously (mTBI group). Rats were imaged with DTI 1 day, 1 week and 12 weeks after impact (Figure 1). A volume-of-interest analysis was performed in the hippocampus for each DTI metric. During training cognitive parameters were extracted: response latency and reward latency for both training tasks, and accuracy for the PAL training and percent premature trials for the CCP training.

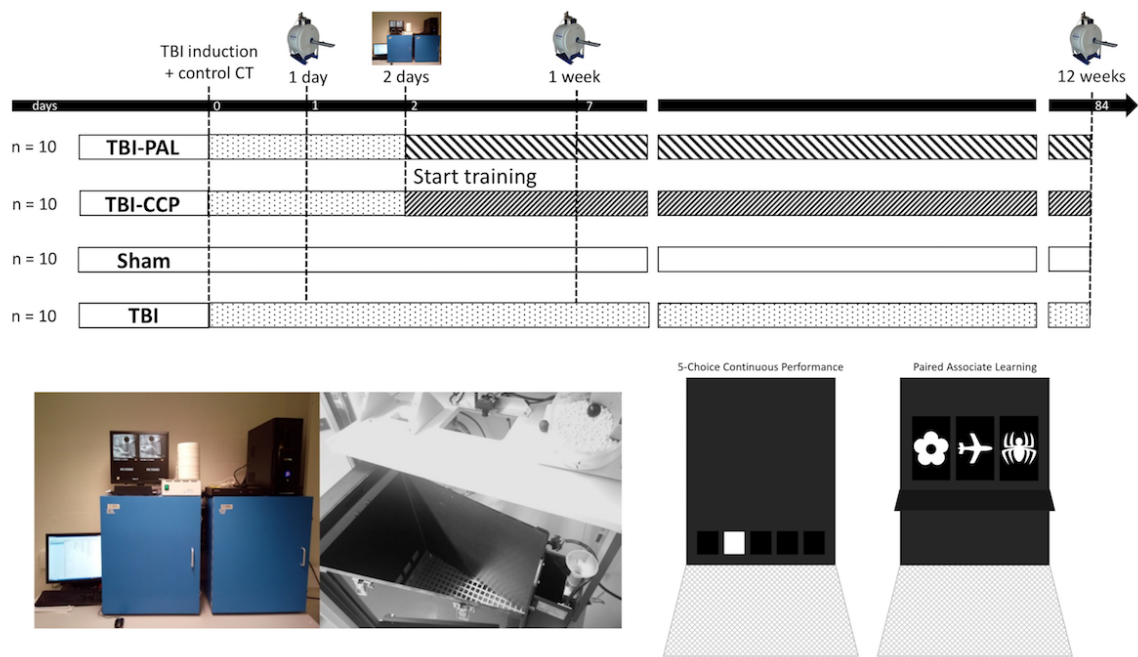
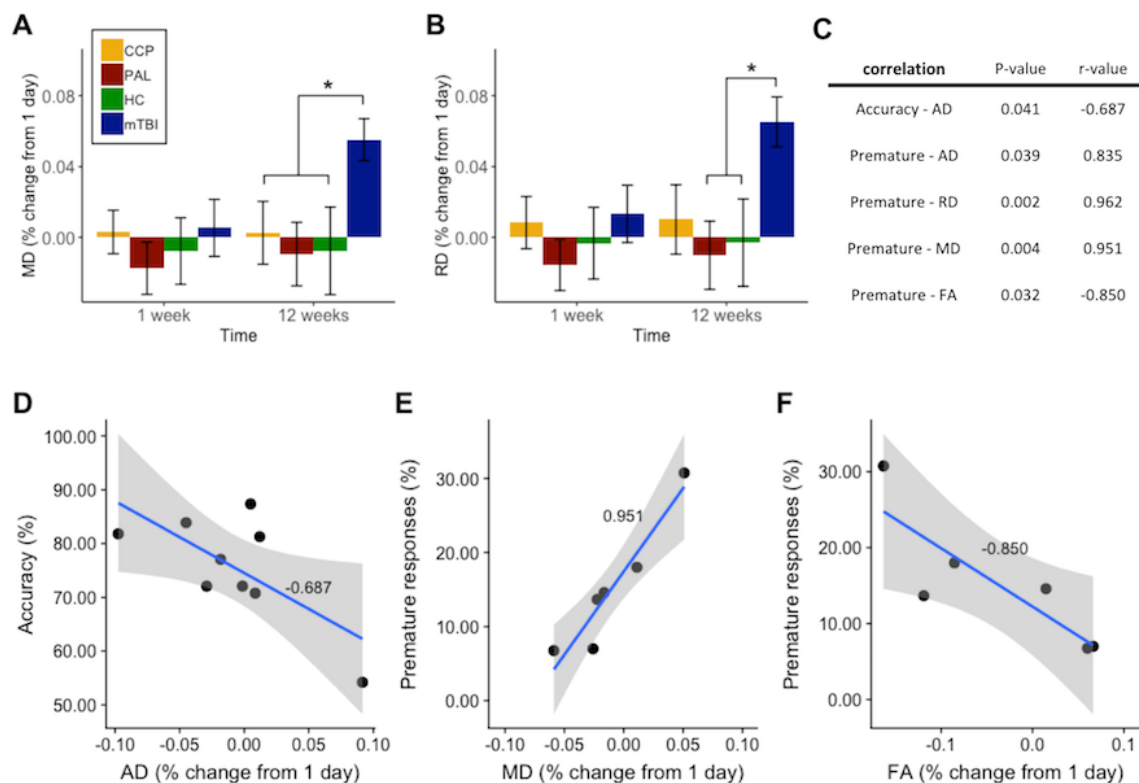


Figure 1. Schematic representation of the study design (top). On the bottom left the Bussey-Saksida Touchscreen training boxes and a schematic representation of the training tasks on the bottom right.

## Results and discussion

Unpaired t-tests revealed that the normalised diffusivity values of the mTBI group were increased compared to the training groups and sham group in the hippocampus 12 weeks post injury (Figure 2, A-B). This increase could be an effect of the breakdown of the brain microstructure and is in line with previous research [4]. On the contrary, the diffusivity in the injured animals with training therapy did not show any change and was comparable with the sham animals. Moreover, we found a significant positive correlation between accuracy and AD in the PAL group (Figure 2, C-D). Also, in the CCP group we found significant correlations between the DTI metrics (AD, RD, MD and FA) and premature responses (Figure 2, C, E-F) indicating that impulsivity is associated with higher diffusivity values and lower FA values. This

further supports our hypothesis that the stable diffusivity values are a result of the training therapy and are beneficial for cognitive functioning.



## Conclusion

Our results provide the first indication of training-induced plasticity in the hippocampus following mTBI in a rat model. Using diffusion MRI, we showed increases in diffusivity in the mTBI group and stable values in the training groups which were associated with better performance and less impulsivity. Based on these neuroimaging findings and correlation analysis, we can be modestly positive about the effect of a training therapy on mTBI.

## References

- [1] M. Majdan, D. Plancikova, A. Brazinova, *et al.*, "Epidemiology of traumatic brain injuries in Europe: a cross-sectional analysis," *Lancet Public Heal.*, vol. 1, no. 2, pp. e76–e83, Dec. 2016.
- [2] J. A. Stephens, K.-N. C. Williamson, and M. E. Berryhill, "Cognitive Rehabilitation After Traumatic Brain Injury," *OTJR Occup. Particip. Heal.*, vol. 35, no. 1, pp. 5–22, 2015.
- [3] K. Caeyenberghs, A. Clemente, P. Imms, *et al.*, "Evidence for Training-Dependent Structural Neuroplasticity in Brain-Injured Patients: A Critical Review," *Neurorehabil. Neural Repair*, vol. 32, no. 2, pp. 99–114, 2018.
- [4] Y. Qin, G. L. Li, X. H. Xu, *et al.*, "Brain structure alterations and cognitive impairment following repetitive mild head impact: An in vivo MRI and behavioral study in rat," *Behav Brain Res*, vol. 340, pp. 41–48, 2018.